Chapter 1

General Introduction

Computational methods have received increasingly more interest for use in investigations of molecular structures and studies of the behaviour and properties of various molecules. Simulation techniques have become an important tool these days to study the three dimensional structures of biopolymers like proteins and DNA. Improvements on protein structure and special purposes such as protein engineering are widely used applications.

The investigation of supramolecular systems containing surface active agents is another field where computation is getting increasingly significant. These substances comprise water- and oil-soluble structure elements and due to this amphipathic character they show surface active properties. Surface activity is of great importance for numerous industrial applications concerning wetting, adhesion, detergency and the like.

Unilever financed the research project described in this thesis, so clearly there is an industrial interest. From an industrial point of view, the development of detergent products for, *e.g.*, cleaning processes, is of great concern. Especially the trend towards more "green" products and milder conditions results in a need for actives of a new generation offering enhanced properties, such as high efficiency at low dosage/low temperature and good biodegradability. In the search and the development of suitable actives it is necessary to study the relationship between the structure of a surfactant and the physico-chemical and macroscopic properties. Computational methods can support the understanding of the mechanisms and the thermodynamics involved in processes such as removal of oily soil from surfaces in the field of detergency.

Aim of research

One of the aims of this research project was to apply the *Molecular Dynamics* computation technique to carbohydrate-based (bio)surfactant and mixed surfactant/water/oil systems for the investigation of structure/function relationships. Another aim was to study the role of surfactant interaction in solution on a molecular and atomic level with respect to their physico-chemical and macroscopic properties (*i.e.*, detergency performance). The combination of these aims resulted in a **characterization of oil/water interfaces**. The term *surfactant* in the context of this thesis is only appropriate for chapter 3. For the other chapters *lipid* is a better description, whereas in the last chapter the word *cosurfactant* is used as well.

Method

Molecular Dynamics (MD) is a well established simulations technique to investigate molecular systems. Over the last two decades, this method has developed rapidly and is well described in the literature. Therefore, to my opinion it is not necessary to go into the details of MD in this

thesis. The people "in the field" always suggest the book of Allen & Tildesley [1] for detailed information and I would also like to suggest the paper of van Gunsteren and Berendsen [2] for a general review on MD methodology, applications and perspectives in chemistry. Recently, the *GROmacs* manual [3] (see the *GROmacs* home page, http://rugmd0.chem.rug.nl/ gmx/gmx.cgi) was written in our group. It gives a clear overview of the method and the force field used in the *GROmacs* package, which we used for several simulations described in this thesis, and is certainly worth reading.

Some of the subjects, like the force fields used, will appear in each chapter because of the "article form"[1] of the chapters. However, in this Introduction I will give the general equations for MD and the force field used. A short MD overview is presented as well, just for the record ...

Equations

In the MD simulation method there is one equation that says it all, Newton's equation of motion:

$$m_i \frac{d^2 \boldsymbol{r}_i(t)}{dt^2} = \boldsymbol{F}_i(\boldsymbol{r}_1, ..., \boldsymbol{r}_N) \tag{1.1}$$

where $\boldsymbol{r}_i$ is the position vector of the particle with mass m_i, and $\boldsymbol{F}_i$ is the force depending on the positions of all (N) particles in the system. The force on particle i is given by the relation:

$$\boldsymbol{F}_i = -\frac{\partial}{\partial \boldsymbol{r}_1} \boldsymbol{V}(\boldsymbol{r}_1, ..., \boldsymbol{r}_N) \tag{1.2}$$

In this equation, $\boldsymbol{V}$ is the interaction potential by which the system is described. The GROMOS [4] and *GROmacs* [3] interaction potential:

$$\begin{aligned} V(\boldsymbol{r}_i) &= V(\boldsymbol{r}_1, ..., \boldsymbol{r}_N) \\ &= \sum V_{bonded}(r) + \sum V_{nonbonded}(r) \end{aligned} \tag{1.3}$$

This can be written as:

$$\begin{aligned} V(r) &= \sum_{n=1}^{N_b} \tfrac{1}{2}\, k_{bond} \left(r - r_{bond}\right)^2 \\ &+ \sum_{n=1}^{N_\theta} \tfrac{1}{2}\, k_\theta \left(\theta - \theta_0\right)^2 \\ &+ \sum_{n=1}^{N_\xi} \tfrac{1}{2}\, k_\xi \left(\xi - \xi_0\right)^2 \\ &+ \sum_{n=1}^{N_\varphi} k_\varphi \left[1 + \cos(n\varphi - \delta)\right] \\ &+ \sum_{i<j}^{N_{at}} \left(4\varepsilon \left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6} \right] + \frac{q_i q_j}{4\pi\varepsilon_0 r} \right) \end{aligned} \tag{1.4}$$

The GROMOS interaction potential (or *force field*) was originally set up for simulations of biomolecules in an aqueous environment. This potential is in fact a typical effective potential

[1] For the interested reader who really reads this thesis from the beginning to the end, I apologize. Because I decided to make this thesis a compilation of articles that resulted from my research project, some items will appear over and over again (although I tried to write it in other words in every chapter).

for a system of N atoms with masses m_i (i=1,2,...,N) and cartesian position vectors r_i. The first term in the potential represents the bond stretching interaction (harmonic potential) along bond r. The minimum energy bond length r_{bond} and the force constant K_{bond} vary with the particular type of bond. The second term is the bond angle (θ) bending interaction and has a similar form. For the dihedral interaction two forms are used: a harmonic term for dihedrals ξ that are not allowed to make transitions (*e.g.*, dihedrals within aromatic rings) and a sinoidal term for the other dihedral angles φ, which are allowed to make 360 degree turns. The last term is a sum over all pairs of atoms and represents the effective nonbonded interaction, composed of the van der Waals and Coulombic interaction between atoms i and j with charges q_i and q_j separated by a distance r_{ij}.

Note, that the molecular models that are used treat all atoms explicitly, except for the hydrogen atoms that are bound to carbon atoms. The CH_n atoms (n=1, 2, or 3) are treated as united atoms, and no special hydrogen-bond potential has been included.

MD overview

It can be helpful to visualize the MD procedure in a flow chart as shown in Figure 1.1. From this scheme it is clear that Newton's equation of motion for the atoms in the system is solved numerically by integration in time. This produces a trajectory of a set of configurations of the system as a function of time. The assumption that the obtained trajectory is statistically representative for the whole phase space is essential. Otherwise several simulations of the same system are needed and this requires much more computer power and time and is therefore not desirable. The simulations describe the microscopic details of a system (like mass and positions of atoms) and by making use of statistical mechanics the macroscopic properties can be calculated and compared with experimental values (density, structural order parameters, diffusion coefficients, etc.).

Outline of this thesis

The outline of the remaining chapters of this thesis is as follows:

Chapter 2 - The decane/water interface

This chapter is the "core" of this thesis, because it describes the effect of the force field parameters (*i.e.*, the van der Waals parameters) on the decane/water surface properties. The study was initiated by the fact that the "old" GROMOS87 parameters [4] produced liquid-liquid interfaces that were too broad. By changing the van der Waals parameters, *i.e.*, varying the Lennard-Jones parameters ϵ and σ between the united CH_2 and CH_3 atoms of the decane molecules and the O-atom of the water molecules, sharper interfaces were obtained. We also compared the two different water models that we use in combination with GROMOS: the SPC [5] and the SPC/E model [6]. The former model turned out to give the best results for the dynamic properties at liquid-liquid interfaces. The results from this study were used to simulate the interfaces described in the other chapters.

Molecular Dynamics

I. Input

Positions $\boldsymbol{r}$ and velocities $\boldsymbol{v}$ of all atoms in the system
Interaction potential V as a function of atom positions

$\Downarrow$

II. Forces

The force on any atom

$$\boldsymbol{F}_i = -\frac{\partial V}{\partial \boldsymbol{r}_i}$$

can be computed by calculating the force between non-bonded atom pairs:

$$\boldsymbol{F}_i = \sum_j \boldsymbol{F}_{ij}$$

plus the forces due to bonded interactions.
Potential/kinetic energies and the pressure are computed.

$\Downarrow$

III. Update

The movement of the atoms is simulated by numerically solving Newton's equation of motion

$$\frac{d^2\boldsymbol{r}_i}{dt^2} = \frac{\boldsymbol{F}_i}{m_i}$$

$\Downarrow$

IV. Output

Positions, velocities, energies, temperature, pressure, etc.

$\Downarrow$

Trajectory in configurational space

$\Downarrow$

Assumption: Set of configurations (ensemble) is statistically representative for the whole phase space

$\Downarrow$

Statistical Mechanics

Microscopic behaviour $\Longrightarrow$ Macroscopic properties

Static: *e.g.*, positions, distances, orientations, correlations
Dynamic: *e.g.*, diffusion, frequencies, relaxation times
Thermodynamic: *e.g.*, density, pressure, viscosity, energy

Figure 1.1: The MD procedure in a flow chart.

Chapter 3 - Carbohydrate based surfactants in surfactant/water/oil systems

This chapter describes simulations of monolayers of two different surfactants at the decane/water interface: α-decyl-glucoside and β-decyl-glucoside, two widely used surfactants in biochemical experiments as well as in detergents. The only difference between the two surfactants is the fact that the α-anomer headgroup is axially oriented towards the apolar tail, whereas the β-anomer has an equatorial orientation. The purpose of this study was to investigate the effect of this difference in orientation of the headgroup on the structural properties of the monolayer. The ultimate goal would of course be the prediction of new compounds to increase the washing performance etc., but for such a purpose one needs more simulations of several surfactants to get a better insight into the behaviour of these surfactants. Unfortunately, this was not feasible at that time. We did obtain nice results, however, and our main conclusion was that the orientation of the headgroup with respect to the tails is very important for the packing of the tail(s) and this is lacking in emperical models for surfactants.

Chapter 4 - Structural properties of DLG in bulk and at the water interface

DLG stands for 1,2-dilauroyl-*sn*-glycerol and is a major component of grease stains in clothing etc. of which not much was known experimentally. We performed four simulations of different DLG systems at 300 and 360 K: a crystal, a pure DLG oil phase, a DLG oil phase in contact with a water layer and an oil/monolayer/water simulation. Our aim was to investigate whether the overall structures of these two types of systems (non-aqueous and aqueous) would converge to the same structure in time. All these systems were simulated for several nanoseconds in total, which was possible thanks to the parallel computer that was situated in our lab and became operational after a long period of testing. Because we performed these long simulations, we were able to take a look at the diffusional properties of these systems and predict the time scales on which these systems equilibrate. This turned out to be in the nanosecond range and we even observed long time diffusion, *i.e.*, DLG molecules diffusing over nanometers on a nanosecond time scale. Although the two types of systems did not converge in time completely, a clear trend towards convergence was observed and we estimated that this would occur within several ns.

Chapter 5 - Characterization of aqueous interfaces with different hydrophobicities

In this chapter we combined the various surface properties of several aqueous interfaces from simulations performed by Siewert Jan Marrink and myself. The systems compared showed a wide range in hydrophobic and hydrophilic components and covered a range of temperatures, but showed very similar properties and surface structures. It turned out that the interfacial width for the hydrophilic components with water was in the range of 1 nm, whereas with the hydrophobic components it was around 0.5 nm. All interfaces have a rough surface as seen by particles of atomic size (0.2 to 0.5 nm), but become smooth, planar surfaces on the nm scale. We also defined a hierarchy of dynamic time scales for various aspects of the surface. From this study we concluded that the interfaces were in a “local” minimum and stable and that the interfaces adjust relatively fast (in tens of ps).

Chapter 6 - Products of hydrolysis at the diglyceride/water interface

Some lipases, that are abundant in nature as well as in washing powders, hydrolyse the ester bonds of glycerides at the glyceride/water interface. The products of the hydrolysis of a diglyceride (like

DLG), are monoglycerides and fatty acids. We studied the effect on the surface properties of these products with increasing concentration and compared it to the pure DLG/water interface of chapter 4. We performed four simulations at 340 K of 2.5 ns each: two with different concentration of monoglycerides and (uncharged or non-dissociated) fatty acids and two simulations with comparable concentrations, but which contained ionized lauric acid and Na^+-counterions. The latter system is a more realistic model and we were interested if the presence of the charges is of influence to the results. This turned out to be of minor importance. The main effects are that these cosurfactants apparently lower the surface tension and increase the total order of all molecules at the interface. Therefore, the interface becomes more flexible and broader and the lipid molecules are presented in a more layered like manner. The cosurfactants do not show a defined clustering behaviour (of, *e.g.*, hydrophilic patches at the interface), but do not form a disperse pattern either. It turned out that defining clustering at interfaces is not that straightforward. However, we observed that the interfaces in this study are more disperse than clustered. The main conclusion from this study was, that these kind of interfaces can rapidly form a template necessary for, *e.g.*, protein binding.

Chapter 7 - Concluding remarks

In this chapter the main results of this thesis are summarized. Also the “state of the art” of MD as a method, with respect to its applications to similar systems, as well as an outlook are discussed.